

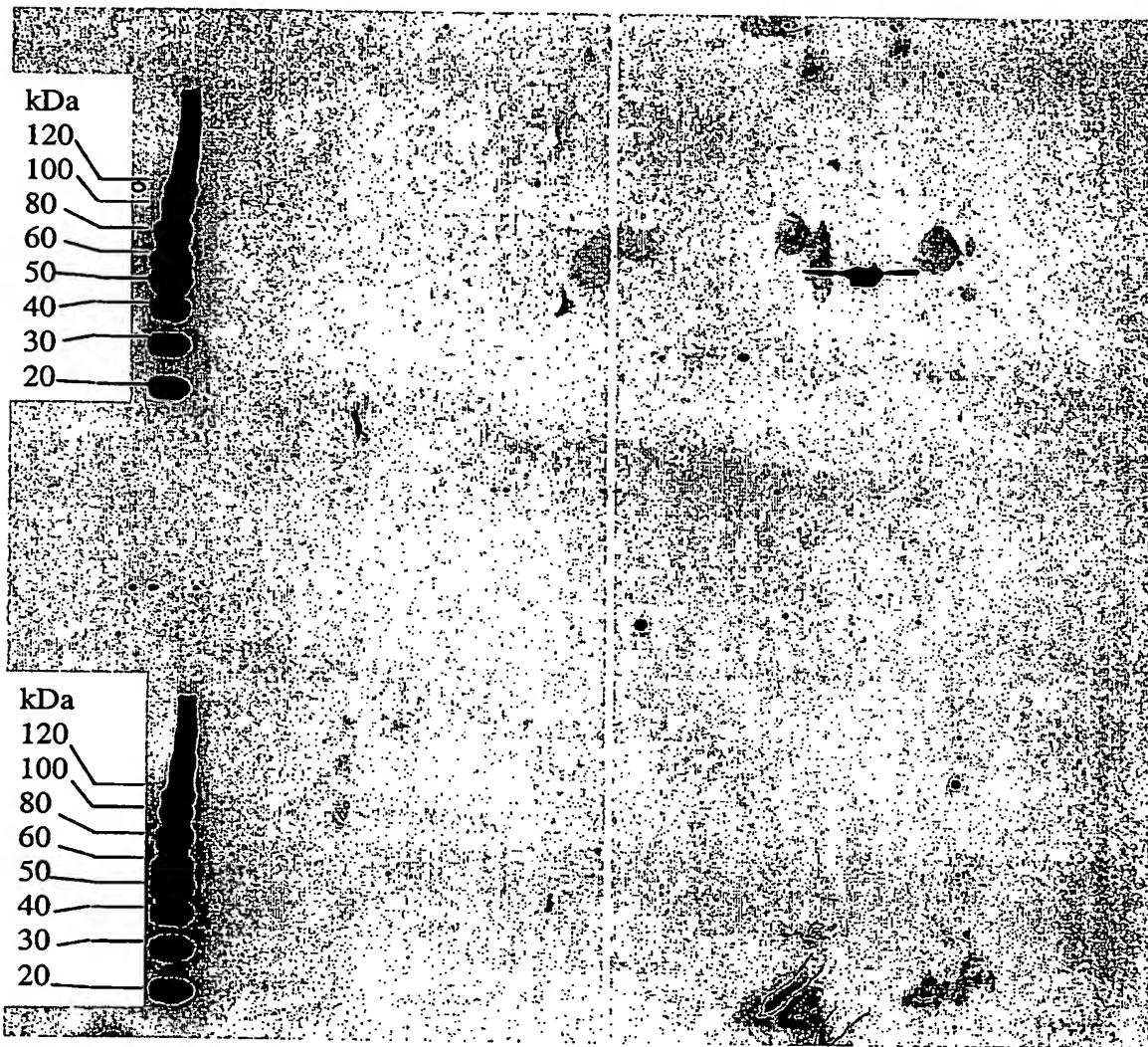
Figure 1 a**Detection of PDE4D7****Media and intima, balloon-injured, left carotis**

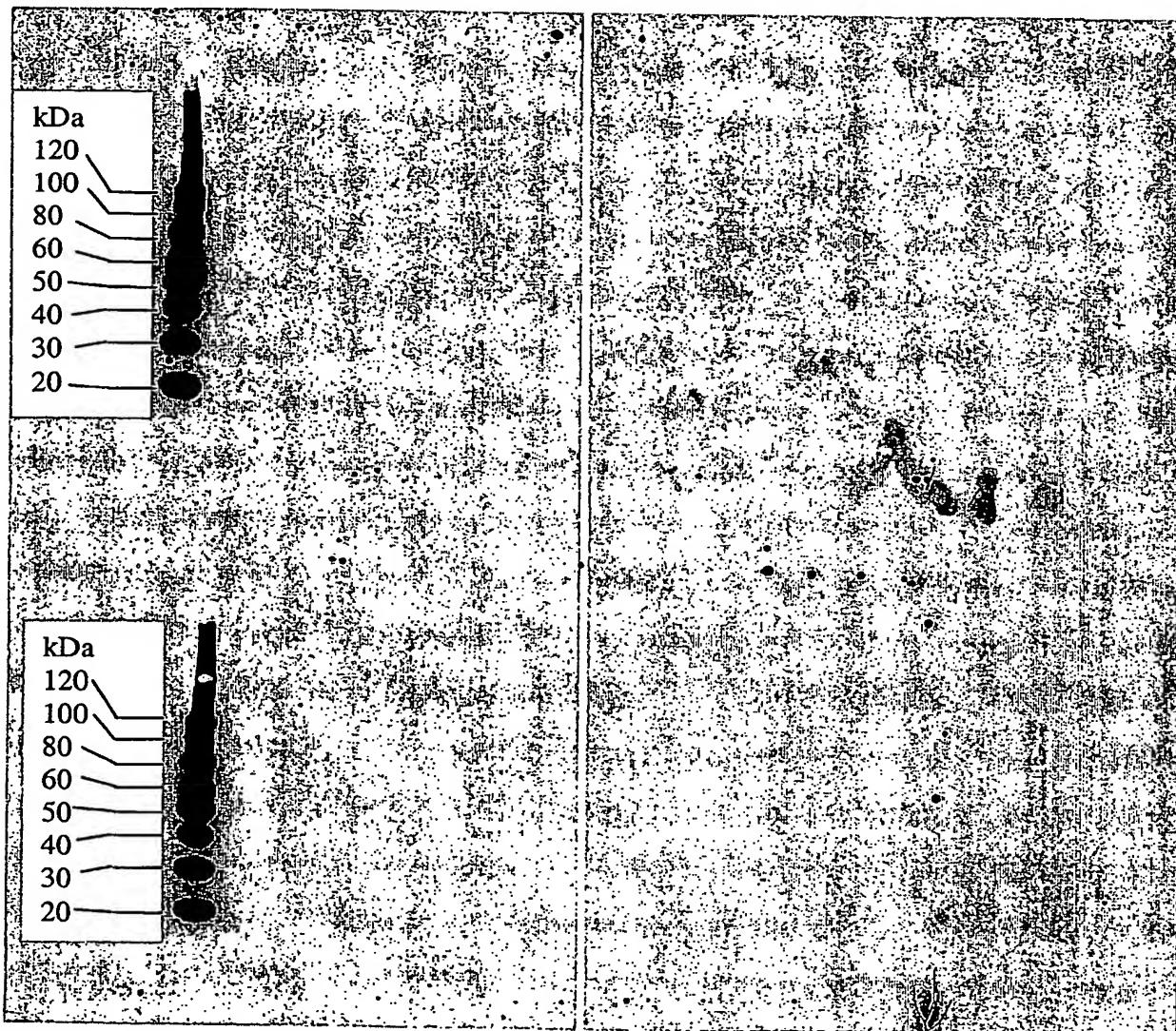
Figure 1 b**Detection of PDE4D7****Media, non-injured, left carotis****Media, non-injured, right carotis**

Figure 2**A. 4D5 N-terminus in man and rat**

4D5 N-terminus: 98.85% identical

HUM.seq x RAT.seq April 1, 2003 17:04 . . .

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1 MAQQ.TSPDTLTVPEDNPHECPNPWLNEGLVKSLSRENLLQHEKSKTARKS 49
||| ||||||||||||||||| ||||||||||||||||| |||||||||||||||||
1 MAQQTTSPDTLTVPEDNPHECPNPWLNEGLVKSLSRENLLQHEKSKTARKS 50

50 VSPKLSPVISPNSPRLLRRMSSNIPKQRRFTVAHT 87
||| ||||||||||||||||| ||||||||||||||||| ||| |
51 VSPKLSPVISPNSPRLLRRMSSNIPKQRRFTVAHT 88

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B. Conserved sequence elements in the human PDE4 gene family

Comparisons:

UCR1

	A	B	C	D
A	+	83.1	79.3	79.7
B		+	79.3	86.4
C			+	86.2
D				+

UCR2

	A	B	C	D
A	+	88.6	78.2	84.8
B		+	79.5	89.9
C			+	83.3
D				+

Catalytic domain

	A	B	C	D
A	+	86.3	82.1	85.2
B		+	80.1	87.4
C			+	84.6
D				+

Figure 3/1

Q8CG05 - Mouse; Q8CG04 - Rat; Q8IVD2 - Human

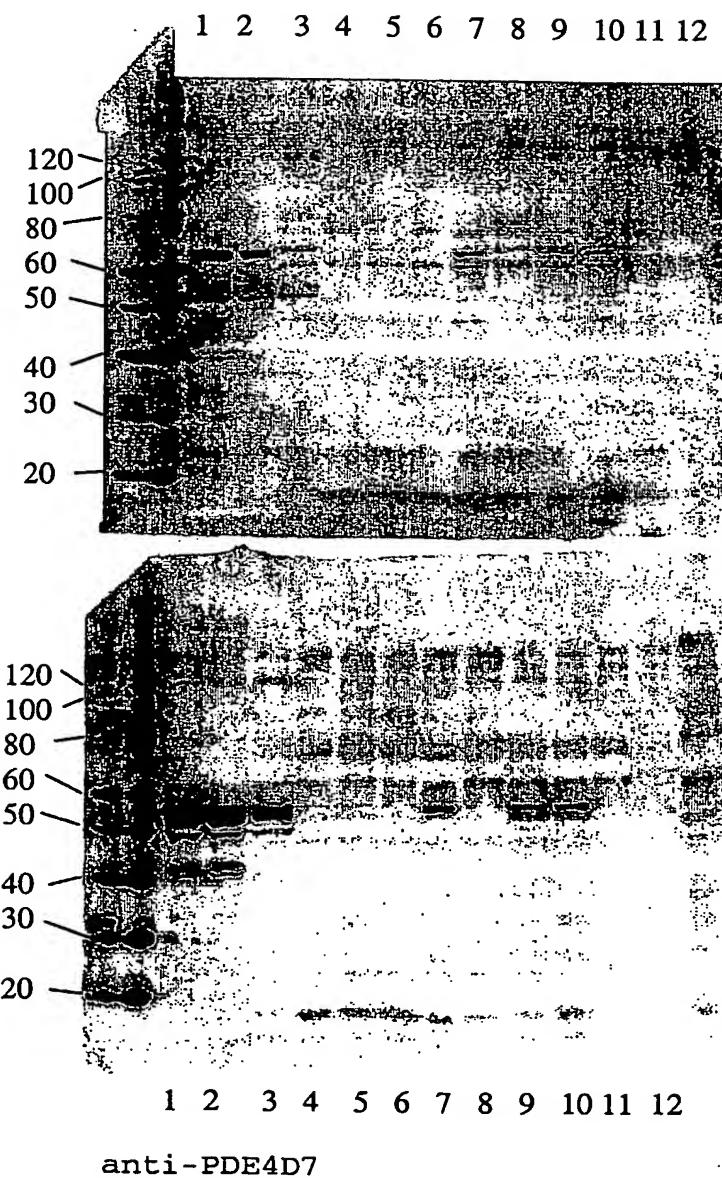
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TR_ROD_Q8CG04	MERNTCDVLS RSKSASEETL HSCNDEEDEPF RGMEPYLVRR LSSRSIQLPP
TR_HUM_Q8IVD2	MKRNTCDLLS RSKSASEETL HSSNEEEDPF RGMEPYLVRR LSCRNQLPP
TR_ROD_Q8CG05	<u>LAFRQLEQAD LRSESENIPR PTSPLKLILP LIAVTSADSS GFDVDNGTSA</u>
TR_ROD_Q8CG04	<u>LAFRQLEQTD LRSESENIPR PTSPLKLILP LIAVTSADST GFDVDNGTSA</u>
TR_HUM_Q8IVD2	<u>LAFRQLEQAD LKSESENIPR PTSPLKLILP LIAITSAESS GFDVDNGTSA</u>
TR_ROD_Q8CG05	GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSRNSS
TR_ROD_Q8CG04	GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSRNSS
TR_HUM_Q8IVD2	GRSPLDPMTS PGSGLILQAN FVHSQRRESP LYRSDSDYDL SPKMSRNSS
TR_ROD_Q8CG05	IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP
TR_ROD_Q8CG04	IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP
TR_HUM_Q8IVD2	IASDIHGDDL IVTPFAQVLA SLRTVRNNFA ALTNLQDRAP SKRSPMCNQP
TR_ROD_Q8CG05	SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM
TR_ROD_Q8CG04	SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM
TR_HUM_Q8IVD2	SINKATITEE AYQKLASETL EELDWCLDQL ETLQTRHSVS EMASNKFKRM
TR_ROD_Q8CG05	LNRELTHLSE MSRSGNQVSE YISNTFLDKQ HEVEIPSPTQ KEKEKKRPM
TR_ROD_Q8CG04	LNRELTHLSE MSRSGNQVSE YISNTFLDKQ HEVEIPSPTQ KEKEKKRPM
TR_HUM_Q8IVD2	LNRELTHLSE MSRSGNQVSE FISNTFLDKQ HEVEIPSPTQ KEKEKKRPM
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TR_ROD_Q8CG04	AELSGNRPLT VIMHTIFQER DLLKTFKIPV DTLITYLMTL EDHYHADVAY
TR_HUM_Q8IVD2	AELSGNRPLT VIMHTIFQER DLLKTFKIPV DTLITYLMTL EDHYHADVAY
TR_ROD_Q8CG05	HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN
TR_ROD_Q8CG04	HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN
TR_HUM_Q8IVD2	HNNIHAADVQ QSTHVLLSTP ALEAVFTDLE ILAAIFASAI HDVDHPGVSN

Figure 3/2

TR_ROD_Q8CG05	QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS
TR_ROD_Q8CG04	QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS
TR_HUM_Q8IVD2	QFLINTNSEL ALMYNDSSVL ENHHLAVGFK LLQEENCDIF QNLTKKQRQS
TR_ROD_Q8CG05	LRKMVIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV
TR_ROD_Q8CG04	LRKMAIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV
TR_HUM_Q8IVD2	LRKMVIDIVL ATDMSKHMNL LADLKTMVET KKVTSSGVLL LDNYSDRIQV
TR_ROD_Q8CG05	LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD
TR_ROD_Q8CG04	LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD
TR_HUM_Q8IVD2	LQNMVHCADL SNPTKPLQLY RQWTDRIMEE FFRQGDRERE RGMEISPMCD
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TR_ROD_Q8CG04	KHNASVEKSQ VGFIDYIVHP LWETWADLVH PDAQDILDTL EDNREWYQST
TR_HUM_Q8IVD2	KHNASVEKSQ VGFIDYIVHP LWETWADLVH PDAQDILDTL EDNREWYQST
TR_ROD_Q8CG05	IPQSPSPAPD DQEEGRQQQT EKFQFELTLE EDCESDTEKD SGSQVEEDTS
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TR_HUM_Q8IVD2	IPQSPSPAPD DPEEGRQQQT EKFQFELTLE EDGESDTEKD SGSQVEEDTS
TR_ROD_Q8CG05	CSDSKTLCTQ DSESTEIPLD EQVEEEAVAE EE.SQPETCV PDDCCPDT
TR_ROD_Q8CG04	CSDSKTLCTQ DSESTEIPLD EQVEEEAVAE EE.SQPQTGV ADDCCPDT
TR_HUM_Q8IVD2	CSDSKTLCTQ DSESTEIPLD EQVEEEAVGE EEESQPEACV IDDRSPDT

Figure 4:

anti-PDE4D5



anti-PDE4D7

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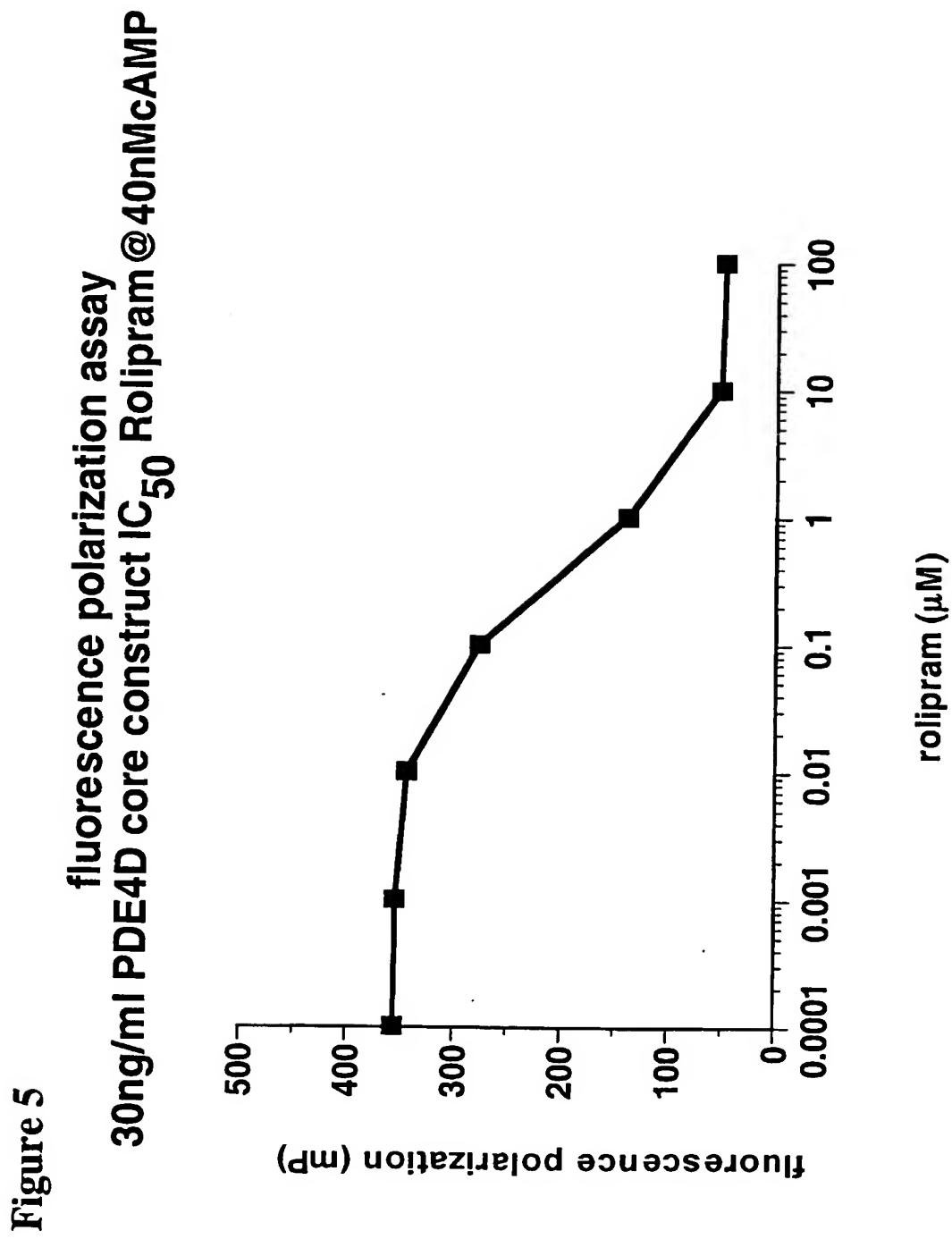


Figure 6

**L/R FEMORAL ARTERY
INJECTION**

TREATMENT (p.o)	
Group 1 (n=12)	Sham operated
Group 3 (n=12)	Lauric Acid (75 µg)
Group 3 (n=12)	Lauric Acid (75 µg)
Group 4 (n=12)	Lauric Acid (75 µg)
	Placebo (vehicle)
	Placebo (vehicle)
	Cilomillast (8 mg/kg/day)*
	Cilostazol (100 mg/kg/day)*

*first dose administered 24 h and 2 h pre-LA injection

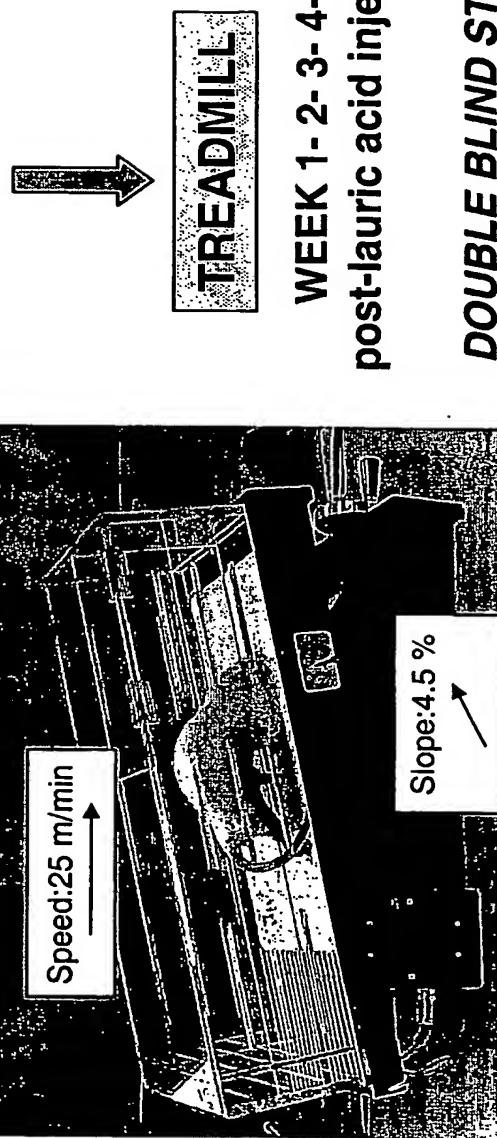


Figure 7

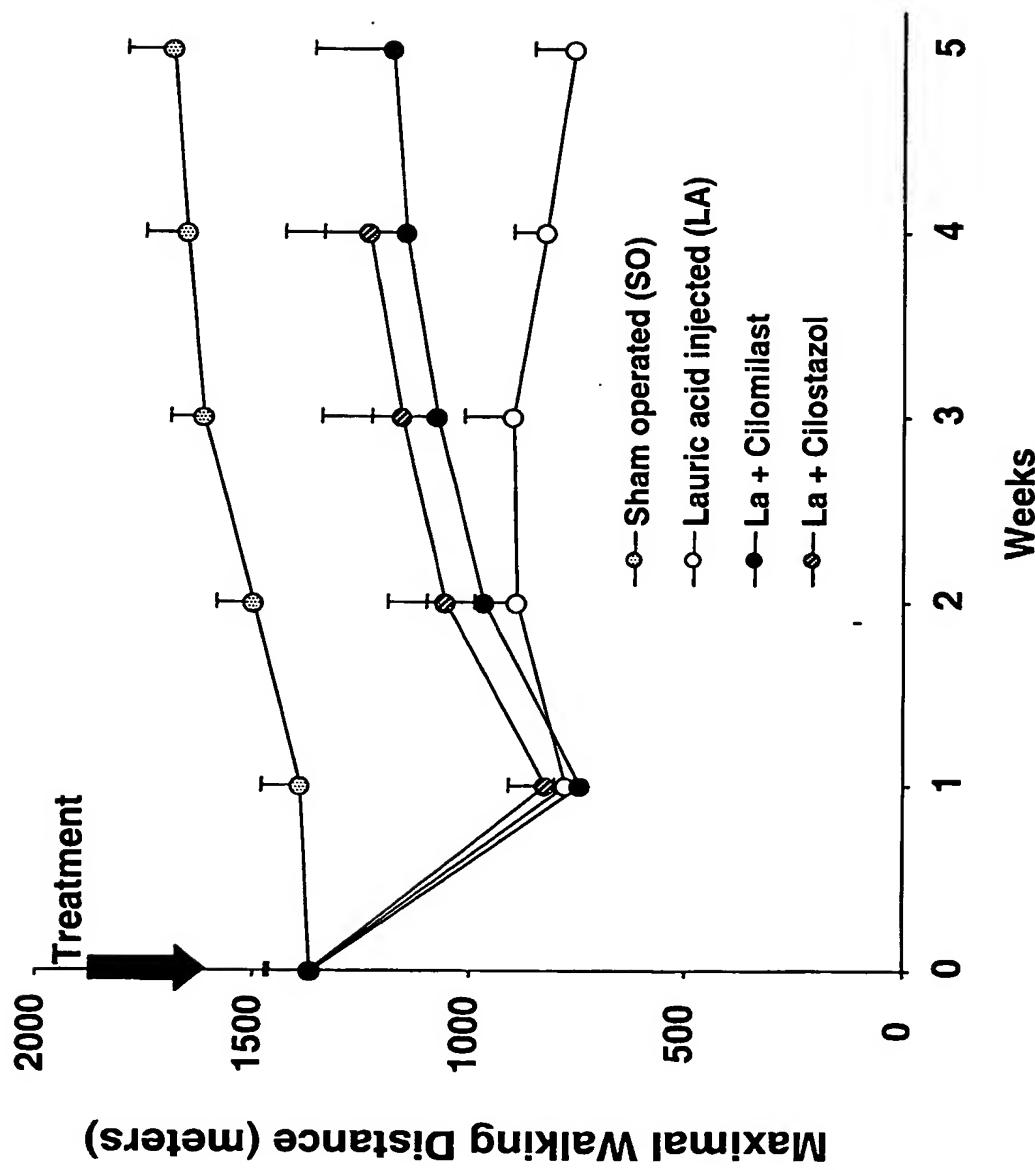
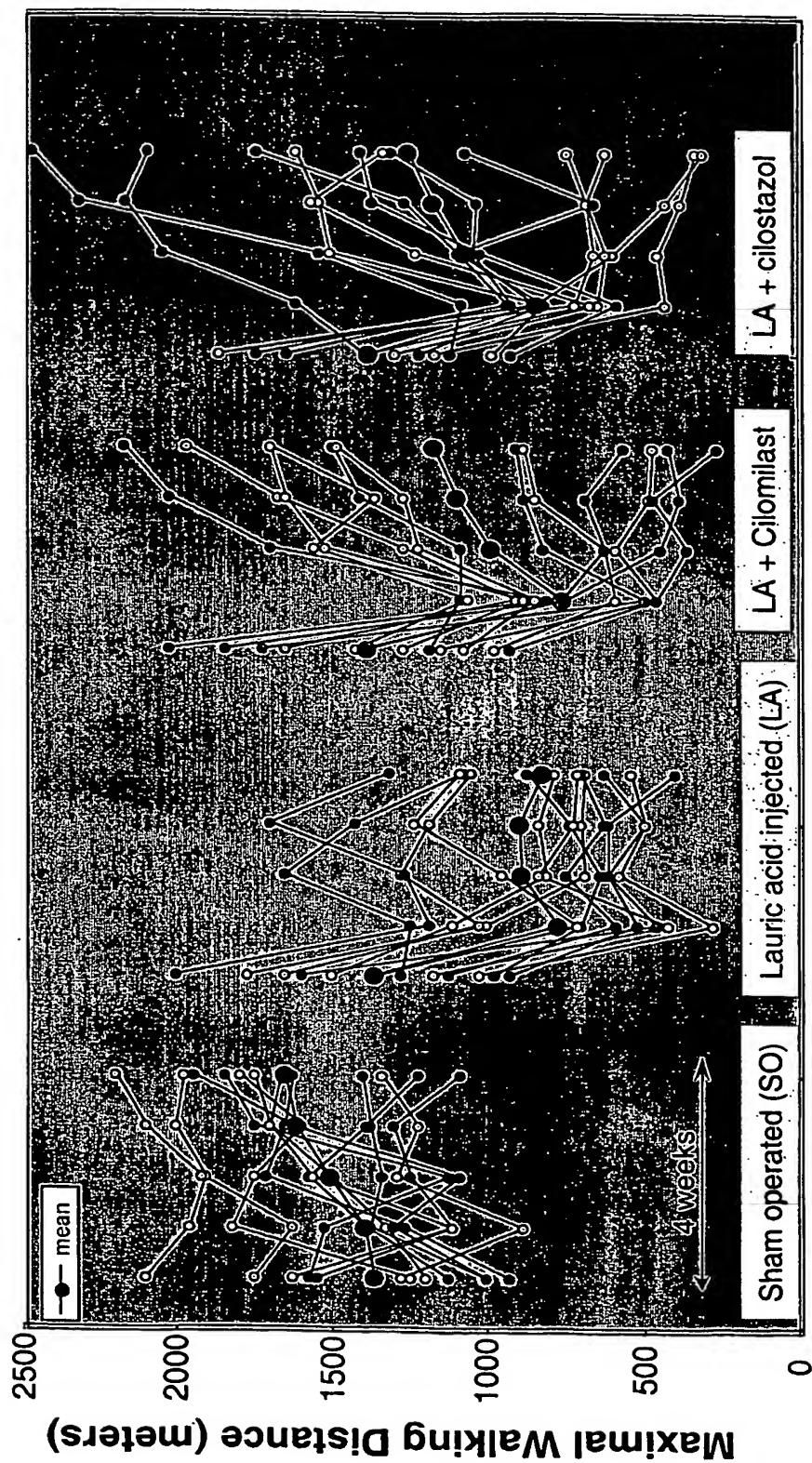


Figure 8
Individual Results*



*N = 12 rats per group

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Figure 9

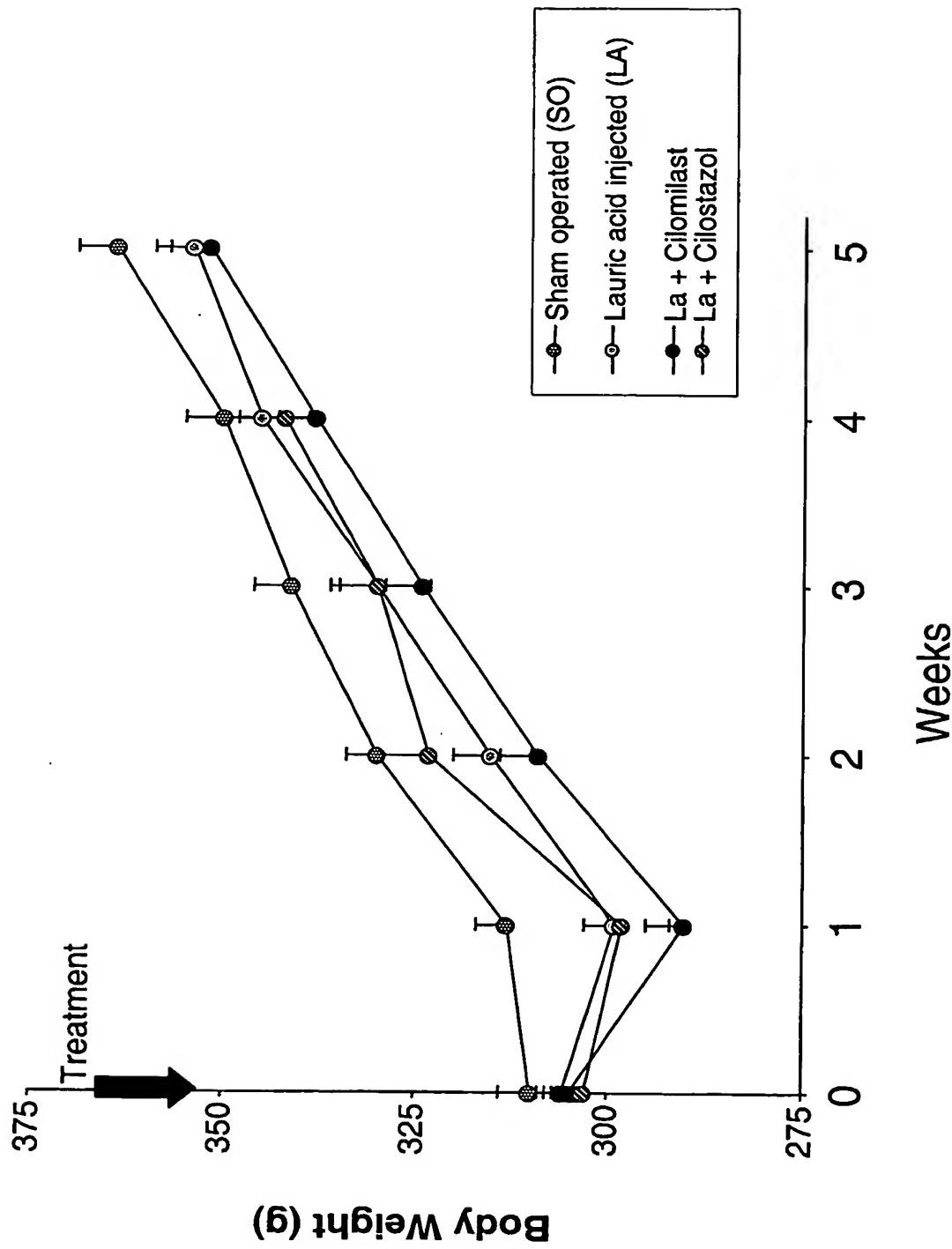
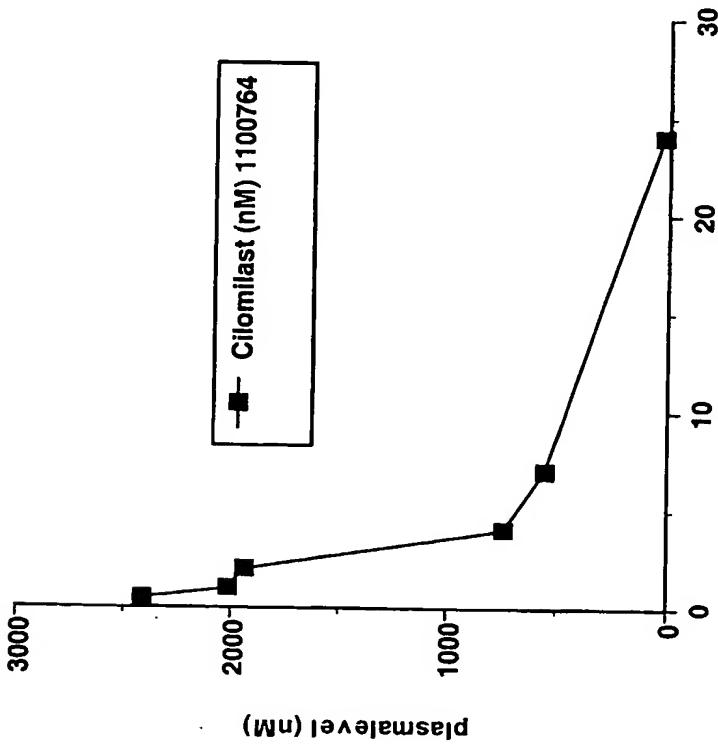


Figure 10

Figure 11

plasmalevel of Cilomilast in rats after oral dosing (lauric acid model)



plasmalevel of Cilomilast in rats after oral dosing

